POS0636

INFLUENCE OF DEMOGRAPHIC AND DISEASE RELATED FACTORS ON EFFICACY OF INFLIXIMAB OR GOLIMUMAB IN RHEUMATOID ARTHRITIS. A META-ANALYSIS ON RANDOMIZED PLACEBO-CONTROLLED TRIALS

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Background: TNF inhibitors have changed the course of rheumatoid arthritis (RA). Yet, detailed analysis on factors influencing clinical response to TNF inhibitors in RA is lacking.

Objectives: Herein we aimed at studying the impact of demographics and disease-related factors on therapeutic response to golimumab and infliximab in RA.

Methods: Randomized clinical trials (RCTs) that evaluated golimumab and infliximab versus placebo or conventional therapy were sought. We selected the following factors: age, sex, ethnicity, body mass index (BMI), smoking status, physical activity, disease duration, disease activity at baseline, presence of auto-antibodies. We studied the impact of these factors on clinical response using firstly aggregate data in a Mantel-Haenszel random effects model, and secondly individual data in a multivariate regression model.

Results: Individual data from 8 RCTs, 2 on infliximab (n=1477) and 6 on golimumab (total =3041) were obtained. In the aggregate model analysis, none of the selected factors had a significant impact on clinical response. In the multivariate analysis, male sex and physical activity were significantly associated with a lower DAS28-CRP after 6 months of treatment (regression coefficients -0.264 (p<0.001) and -0.193 (p=0.004) respectively), while a high initial DAS28-CRP was significantly associated with a higher DAS28-CRP (regression coefficient 0.579 (p<0.001)). The baseline disease activity was the only significant interaction factor with the effect of the treatment.

Conclusion: Male gender and practicing physical activity are associated with lower disease activity 6 months after golimumab or infliximab initiation. High baseline disease activity significantly influences negatively the effect of the treatment on disease activity score.

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POS0637

INCIDENCE AND DETERMINANTS ASSOCIATED WITH RETRANSITIONING FROM BIOSIMILAR SB4 TO ORIGINATOR ETANERCEPT

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Background: The market entry of the etanercept biosimilar SB4 (BS-ETA) reduced prices; and, therefore, many patients in clinical practice are transitioned from originator etanercept (OR-ETA) to BS-ETA. However, previous studies demonstrated that 2.7-17.1% of patients who transitioned from OR-ETA to BS-SB4, retransitioned to OR-ETA (i.e. restarted originator), which might reduce

the (financial) benefits of biosimilars. Insight in the incidence of retransitioning and characteristics of patients who are most likely to retransition, can provide lessons to clinicians for successful introduction of biosimilars.

Objectives: To assess the incidence of retransitioning from BS-ETA to OR-ETA in patients with a rheumatic disease (RD) and to identify determinants thereof.

Methods: All patients diagnosed with RD who transitioned in 2016 from OR-ETA to BS-ETA in a Dutch general teaching hospital (the Spaarne Gasthuis, Haarlem/Hoofddorp) were included in this cohort study. All patients were followed until retransitioning, switching to another biological, discontinuing of biological treatment death, loss to follow up or until censor date. The incidence of retransitioning and duration of BS-ETA use was assessed using the Kaplan-Meier method. Potential determinants for retransitioning, including age, gender, BS-SB4 dosing interval, use of other biologicals prior to OR-ETA, initiation or intensification of corticosteroids or immunomodulators, hospitalisations and the number of outpatient visits to the rheumatology department, were assessed in a nested case control study, using (multivariate) conditional logistic regression.

Results: In total, 342 patients (median age 57.8 years, 53.5% females, median follow-up 2.7 years) were included. 9.4% of patients had retransitioned to OR-ETA one year after transitioning. Additionally, one year after transitioning 69.7% of patients were still treated with BS-ETA, 3.8% switched to other treatment and 17.1% discontinued all biological treatment. At the end of follow-up (median 2.7 years), 46 patients (13.5%) retransitioned to OR-ETA; median time until retransitioning was 0.50 (IQR 0.98) years.

Univariate determinants for retransitioning included female gender (OR 2.37, 95% CI 1.18-7.74), initiating or intensifying corticosteroids or immunomodulators (OR 3.24, 95% CI 1.38-7.63) and number of visits to the rheumatology department (OR 2.32, 95% CI 1.70-3.17). Based on the multivariate analysis, only the number of visits to the rheumatology department was associated with retransitioning (OR 2.19 95% CI 1.60-3.00), as demonstrated in Table 1.

Conclusion: When introducing BS-SB4 in clinical care, clinicians should anticipate on about one in seven patients retransitioning to OR-ETA. These patients might be identified prior to retransitioning based on their contacts to the rheumatology department. Information specifically aiming for their concerns might prevent them from retransitioning. However, more qualitative studies are needed to explore patients' underlying reasons for retransitioning, in order to improve the introduction of biosimilars in clinical care.

Table 1. Determinants for retransitioning

	Cases n = 46	Controls n = 184	OR (univariate) 95% CI	OR (multivariate) 95% CI
Age, years (median, IQR)	59.0 (16.5)	56.5 (22.3)	1.01 (0.98–1.03)	-
Gender				
Male	15 (32.6%)	97 (52.7%)	Ref	Ref
Female	31 (67.4%)	87 (47.3%)	2.37 (1.18–7.74)	1.36 (0.60–3.07)
BS-SB4 dosing interval (index date)				
7 days	35 (76.1%)	129 (70.1%)	Ref	-
>7 days	11 (23.9%)	55 (29.9%)	0.72 (0.33–1.56)	
Previous use other biological				
No	43 (93.5%)	172 (93.5%)	Ref	-
Yes	3 (6.5%)	12 (6.5%)	1.00 (0.27–3.74)	
Initiation/ intensification corticosteroid/ immunomodulator				
No	35 (76.1%)	168 (91.3%)	Ref	Ref
Yes	11 (23.9%)	16 (8.7%)	3.24 (1.38–7.63)	2.31 (0.84–6.38)
Hospitalisation				
No	41 (89.1%)	166 (90.2%)	Ref	-
Yes	5 (10.9%)	18 (9.8%)	1.12 (0.40–3.18)	
No. visits rheumatology department (median, IQR)	2 (2)	0 (1)	2.32(1.70–3.17)	2.19 (1.60–3.00)

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POS0638

DISEASE SEVERITY AND OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVE A NEWLY APPROVED BIOLOGIC: REAL-WORLD US EXPERIENCE WITH SARILUMAB FROM THE ACR RISE REGISTRY

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Background: Patients with rheumatoid arthritis (RA) who have received multiple biologics or targeted therapies over time tend to have more refractory and more severe disease, which may lead to worse clinical response to treatment.

Objectives: We used data from the ACR RISE registry to assess whether disease severity was greater in those who received sarilumab shortly after its FDA approval (May 2017) than in subsequent time periods and to evaluate the effectiveness of sarilumab in populations with various degrees of disease severity.

Methods: Patients with RA who initiated sarilumab treatment in the period 2017-2020 were identified in the ACR RISE registry and divided into Cohort 1 (2017, year of the FDA approval) and the calendar year-based Cohorts 2-4 (2018-2020). Patient demographics, RA-related features, and comorbidities were determined using data prior to sarilumab initiation. The cohorts were compared using chi-square test (categorical variables) and a nonparametric test (continuous variables). Sarilumab effectiveness was assessed using 3 cohorts assembled based on progressively restrictive criteria: Active Disease cohort (Clinical Disease Activity Index [CDAI] >10 or Routine Assessment of Patient Index Data 3 [RAPID3] >6, and C-reactive protein, if measured, ≥ 8 mg/L), TARGET Eligibility cohort (patients who satisfied enrolment criteria for TARGET,¹ a Phase 3 sarilumab trial in patients with RA and an inadequate response to TNF inhibitors), and TARGET Baseline cohort (patients from TARGET Eligibility cohort with characteristics weighted to match those from the TARGET trial baseline,¹ using the matching-adjusted indirect comparison method²). In all 3 effectiveness cohorts, mean changes in CDAI and RAPID3 at 6 and 12 months post-initiation of sarilumab were evaluated using a model adjusted for baseline score, age, sex, race, calendar year, and seropositivity.

Results: A total of 2949 patients, treated by 585 rheumatologists, initiated sarilumab treatment in the period 2017–2020. The 4 yearly cohorts were relatively similar in terms of patients' age, sex, race, and most clinical characteristics. However, patients receiving sarilumab shortly after FDA approval (Cohort 1) had more ambulatory visits, a greater number of previously used non-TNFi biologics (particularly tocilizumab), and a higher comorbidity burden, and were more likely to be current users of glucocorticoids or opioids than sarilumab initiators in the subsequent 3 years. In the 3 cohorts used to assess sarilumab effectiveness, the greatest improvement was observed in the TARGET Baseline cohort, which also had the greatest mean baseline CDAI score (43), compared with the other two (24 both).

Conclusion: In this real-world cohort, we observed modest evidence for channeling of patients with greater RA severity and greater prior exposure to non-TNFi biologics to sarilumab shortly after its FDA approval. This cohort effect did not diminish the effectiveness of sarilumab. All cohorts showed improvement, with the greatest clinical improvement observed in the cohort with the highest baseline CDAI score who most closely resembled those enrolled in a phase 3 trial of patients with an inadequate response to TNF inhibitors.

REFERENCES:

- [1] Fleischmann R, et al. *Arthritis Rheumatol* 2017;69:277-290.
- [2] Signorovitch JE et al. *Value Health* 2012;15:940-7.

Figure 1. Adjusted improvements in CDAI and RAPID3

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POS0639

LONG-TERM EFFECTIVENESS OF THE RITUXIMAB HALF DOSE REGIMEN FOLLOWING A RESPONSE TO THE LICENSED DOSE IN RHEUMATOID ARTHRITIS

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Background: Following initial treatment with rituximab (RTX) full dose (2x1000mg), B-cell numbers are often lower than baseline. The half dose regime (2x500mg) has been reported to be similarly effective [1]; however, there is limited long-term data on the effectiveness of switching to RTX half-dose from the real-world perspective.

Objectives: To compare the 3-year RTX regime retention between patients receiving retreatment with half-dose and full-dose of RTX, and assess factors associated with maintenance of 2x500mg, with a view to establish an optimal long-term retreatment strategy in RA.

Methods: An observational study was conducted on 755 consecutive RTX-treated RA patients in a single centre for over 20 years. Of these, 165/755 (22%) received at least one cycle of 2x500mg. Long-term effectiveness was assessed using RTX retention rate. Drug survival of patients treated with 2x500mg was compared with 200 RA patients receiving 2x1000mg throughout the study, matched to the number of cycle when the 2x500mg regime was initiated.

Results: Of the 165 patients who received 2x500mg, 81.8% were female; mean age was 63.4 (26-91) years; mean disease duration 15.5 (2-53) years; 57 (34.5%) were bDMARDs-naïve; 121 (74%) were on concomitant DMARDs and mean DAS-28 was 3.9 (SD 1.29) at the half dose initiation. At 3 years, the retention rate was 38% for patients receiving 2x500mg compared to 87% for those on 2x1000mg; HR for half dose discontinuation was 6.17 [95%CI (3.91-12.27); p<0.001] (Figure 1A).

The main reasons for 2x500mg discontinuation were poor EULAR response (30%); moderate EULAR response (30%); shorter duration of response compared to the full dose (22%); and incomplete B-cell depletion (17%). The majority of these patients (87.9%) were switched back to 2x1000mg, 5.1% received other bDMARDs and 7.1% did not receive further DMARDs.

In multivariable analysis, previous TNFi use was associated with 3-year maintenance of the 2x500mg dose [OR 2.63 (1.12-6.10); p=0.024]; while higher plasmablasts at 2x500mg initiation was associated with shorter maintenance of this regime [OR 0.78 (0.67-0.97); p=0.028].

There were no significant differences in 5-year RTX retention rates between patients receiving 2x500mg and switched back to 2x1000mg vs those receiving 2x1000mg throughout the study (Log-Rank=0.186) (Figure 1B).

Conclusion: The use of RTX half-dose regimen was associated with poor retention at 3 years. Nevertheless, where loss of effectiveness occurs post-2x500mg initiation, switching back to 2x1000mg appears to be a pragmatic option. Patients with previous TNFi exposure and lower plasmablasts may be most suited to be commenced on the 2x500mg dose for long-term disease control.

REFERENCES:

- [1] Mariette X, et al. *ARD* 2014